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Docket No.: PA-0028 US

Certificate of Mailing

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on June 7, 2002

__ Printed: _

Debbie Ellis

WIER 1600/28

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Olga Bandman

Title:

GENES DIFFERENTIALLY EXPRESSED IN VASCULAR TISSUE

ACTIVATION

Serial No.:

10/044,090

Filing Date:

January 08, 2002

Examiner:

To Be Assigned

Group Art Unit:

1636

Commissioner for Patents Office of Initial Patent Examination Customer Service Center Washington, D.C. 20231

REQUEST FOR A CORRECTED FILING RECEIPT

Sir:

Attached is a copy of the Official Filing Receipt (with red-line markings to note changes) received from the United States Patent and Trademark Office (USPTO) in the above application for which issuance of a corrected filing receipt is respectfully requested. Please make the correction as follows:

1. Under the Section entitled "Domestic Priority data as claimed by applicant," please replace "THIS APPLN CLAIMS BENEFIT OF 60/222,469 07/28/2000 AND CLAIMS BENEFIT OF 60/260,483 01/08/2001" with --THIS APPLN CLAIMS BENEFIT OF 60/260,483 01/08/2001--.

Applicants hereby request that the above corrections be entered based on the following enclosed documents:

- 1. Copy of executed Declaration and Power of Attorney (3 pp.). submitted May 3, 2002; and
- 2. Copy of first page of application Specification.

Docket No.: PA-0028 US

Applicants believe that no fee is due with this paper. However, if the Commissioner determines that a fee is necessary, the Commissioner is hereby authorized to charge any additional fees associated with this communication or credit any overpayment to Deposit Account No. **09-0108.**

Respectfully submitted,

INCYTE GENOMICS, INC

Lynn E. Murry, Ph.D.

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Printed: Debbie Ellis Docket No.: PA-0028 US IN THE UNITED STATES PATENT AND TRADEMARK OFFICE In re Application of: Olga Bandman Title: GENES DIFFERENTIALLY EXPRESSED IN VASCULAR TISSUE ACTIVATION Serial No.: 10/044,090 Filing Date: January 08, 2002 Examiner: To Be Assigned Group Art Unit: 1636

Commissioner for Patents Office of Initial Patent Examination Customer Service Center Washington, D.C. 20231

TRANSMITTAL FEE SHEET

Sir:

Transmitted herewith are the following for the above-identified application:

- 1. Return Receipt Postcard;
- 2. Request for Corrected Filing Receipt (2 pp.);
- 3. Copy of official Filing Receipt (with red-lined markings) (1 pg.);
- 4. Copy of executed Declaration and Power of Attorney (3 pp.), submitted May 3, 2002; and
- 5. Copy of first page of application Specification.

The fee has been calculated as shown below.

X No additional Fee is required.

Please charge Deposit Account No. 09-0108 in the amount of :

\$

The Commissioner is hereby authorized to charge any additional fees required under 37 CFR 1.16 and 1.17, or credit overpayment to Deposit Account No. 09-0108. A duplicate copy of this sheet is enclosed.

Respectfully submitted,

INCYTE GENOMICS, INC.

Lynn E. Murry, Ph.D.

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tes Patent and Trademark Office

COMMISSIONER FO UNITED STATES PATENT AND TRADEMAR WASHINGTON

APPLICATION NUMBER FILING DATE GRP ART UNIT FIL FEE REC'D ATTY.DOCKET.NO DRAWINGS TOT CLAIMS 10/044,090 01/08/2002 1636 870 PA-0028 US 20

27904 INCYTE GENOMICS, INC. 3160 PORTER DRIVE PALO ALTO, CA 94304

CONFIRMATION **UPDATED FILING RECEIPT** *OC000000008259712*

COPY OF PAPERS ORIGINALLY FILED

Date Mailed: 06/10/2002

Receipt is acknowledged of this nonprovisional Patent Application. It will be considered in its order and you will be notified as to the results of the examination. Be sure to provide the U.S. APPLICATION NUMBER, FILING DATE, NAME OF APPLICANT, and TITLE OF INVENTION when inquiring about this application. Fees transmitted by check or draft are subject to collection. Please verify the accuracy of the data presented on this receipt. If an error is noted on this Filing Receipt, please write to the Office of Initial Patent Examination's Filing Receipt Corrections, facsimile number 703-746-9195. Please provide a copy of this Filing Receipt with the changes noted thereon. If you received a "Notice to File Missing Parts" for this application, please submit any corrections to this Filing Receipt with your reply to the Notice. When the USPTO processes the reply to the Notice, the USPTO will generate another Filing Receipt incorporating the requested corrections (if

Applicant(s)

Olga Bandman, Mountain View, CA:

Domestic Priority data as claimed by applicant

THIS APPLN CLAIMS BENEFIT OF 60/222,469 07/28/2000 AND CLAIMS BENEFIT OF 60/260,483 01/08/2001

Foreign Applications

If Required, Foreign Filing License Granted 03/06/2002

Projected Publication Date: 09/19/2002

Non-Publication Request: No

Early Publication Request: No

Title

Genes differentially expressed in vascular tissue activation

Preliminary Class

435

EXPRESS MAIL NO. EL 856 173 7154

COPY OF PAPERS ORIGINALLY FILED

DA-0028 US

US
GENES DIFFERENTIALLY EXPRESSED IN VASCULAR.

This application claims the benefit of United States provisional application Serial No.60/266,483 8 January 2001.

The present invention relates to a combination comprising a plurality of cDNAs which are differentially expressed in activated vascular tissue and which may be used entirely or in part to diagreese, to stage, to treat, or to monitor the progression or treatment of disorders such as atherosclerosis.

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BACKGROUND OF THE INVENTION

Atherosclerosis is a pathological condition characterized by a chronic local inflammatory response within the vessel wall of major arteries. Disease progression results in the formation of atherosclerotic lesions, unstable plaques which occasionally rupture, precipitating a catastrophic thrombotic occlusion of the vessel lumen. Atherosclerosis and the associated coronary artery disease and cerebral stroke represent the most common causes of death in industrialized nations. Although certain key risk factors have been identified, a full molecular characterization that elucidates the causes and identifies all potential therapeutic targets for this complex disease has not been achieved. Molecular characterization of atherosclerosis requires identification of the genes that contribute to lesion growth, stability, dissolution, rupture and induction of occlusive vessel thrombi.

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Blood vessel walls are composed of two tissue layers: an endothelial cell (EC) layer which comprises the lumenal surface of the vessel, and an underlying vascular smooth muscle cell (VSMC) layer. Through dynamic interactions with each other and with surrounding tissues, the vascular endothelium and smooth muscle tissues maintain vascular tone, control selective permeability of the vascular wall, direct vessel remodeling and angiogenesis, and modulate inflammatory and immune responses.

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The inflammatory response is a complex vascular reaction mediated by numerous cytokines, chemokines, growth factors, and other signaling molecules expressed by activated ECs, VSMCs and leukocytes. Inflammation protects the organism during trauma and infection, but can also lead to pathological conditions such as atherosclerosis. The pro-inflammatory cytokines, interleukin (IL)-1 and tumor necrosis factor (TNF), are secreted by a small number of activated macrophages or other cells and can set off a cascade of vascular changes, largely through their ability to alter gene expression patterns in ECs and VSMCs. These vascular changes include vasodilation and increased permeability of microvasculature, edema, and leukocyte extravasation and transmigration across the vessel wall. Ultimately, leukocytes, particularly neutrophils and monocytes/macrophages, accumulate in the extravascular space, where they remove injurious agents by phagocytosis and oxidative killing, a process accompanied by release of toxic factors, such as proteases and reactive oxygen species.

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